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Jill Castellano <jillcastellano@inewsource.org>

Journalist writing about inaccurate information in your research papers

Kang Zhang <kang.zhang@gmail.com> Wed, Jul 17, 2019 at 10:34 AM
To: jillcastellano@inewsource.org

Dear Ms. Castellano,

It is not unusual for groundbreaking research involving innovative treatments to invite criticism, especially from persons who are wed to the pre-existing treatments. There is a forum for suchcriticism of peer-reviewed articles, and the response, in the academic journals in which the research is published. That forum was used and a healthy dialogue ensued about the study about which you have invited comment. Please note the comments published by these two ophthalmologist groups and our response have been rigorously adjudicated and approved by a panel of world's top experts in this field invited by Nature, who also reviewed and approved our initial publication.

A team of researchers worked on the study, not just me. You will note that I was not listed as the first or last author which are the positions reflecting the largest contributions. But I, and, I believe, the entire team would stand by the quality of the research notwithstanding the criticism. I believe you are, or should be, in touch with at least Doctor Liu and Dr. Maas, who I believe are quite willing to address your questions about the study.

The study was not "unethical, misleading, or dangerous." The study followed international standards and requirements for clinical trials and received appropriate Institutional Review Board oversight.

Performing surgeries on both eyes of the patients was a thoughtful decision and was done to prevent an imbalance of vision and increased risk of amblyopia, as explained by Dr. Liu.

You have been misled if you have been told that animal testing did not precede human testimony. Safety and efficacy were established with rabbits and monkeys prior to studying the procedure on human patients.

The insinuation that the results were somehow inaccurate was addressed (and debunked) by the research team in response to the same criticism leveled in Nature. The response included the following:

> While these lenses were mostly clear (particularly in the visual axis), we did not claim that they were completely normal and explicitly acknowledged their imperfections, which mainly reflected loss of LECs, mild peripheral scarring at the capsulorhexis site, and anterior–posterior capsule adhesions that resolve over time. The histopathology sections interpreted by Vavvas et al. as showing small or irregular lenses were intentionally cut offset from the axial centre of the lens to minimize disruption to the lens cortex. Furthermore, dissected lenses often shrink upon alcohol dehydration. Thus, irregularities in size or shape were essentially fixation artefacts.
>
> Regarding visual outcomes, the studies cited by Vavvas et al. are not comparable to ours for several reasons. First, the mean age was higher (5.3 years and 10.2 years compared with under 2 years in our study), which may have confounded visual outcomes, as the IATS noted that follow-up length can affect visual acuity comparisons4. Second, the evaluation of visual acuity differed (Teller Acuity Cards for visual resolution versus Snellen Visual Acuity

for visual recognition). Although Teller cards can be roughly translatable to Snellen equivalents, accuracy and false comparison concerns usually preclude this.

In commenting on our outcomes, Solebo et al.did not account for normal age-related changes in visual acuity. During development, 20/200 is close to normal vision for six months of age, and 20/50–20/80 is close to normal vision for one year of age, depending upon the method of testing used. The visual acuity levels in our population were appropriate and not inferior to their results if age is appropriately considered. In addition, an error in vision reported in our initial paper was corrected in a subsequent Corrigendum. Therefore, their comments on our visual acuity results are now out of context and inaccurate.

The research was properly conducted and it supported both a new approach to the treatment of cataracts and a new paradigm for using stem cells in enabling humans to regenerate tissue. It thereby revealed an immense potential for alleviating suffering and improving the quality of life for countless people well beyond the field of ophthalmology.

Thank you for allowing me to respond to your questions.

Kang Zhang, MD, PhD

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Jill Castellano <jillcastellano@inewsource.org>

UCSD review process

Kang Zhang <kang.zhang@gmail.com> Sun, Jul 21, 2019 at 12:32 AM
To: Jill Castellano <jillcastellano@inewsource.org>

Dear Ms. Castellano,
Thank you for your email and for following up regarding the human subject study discussed in the *Nature* article. Your reference to that human subject study as "your study" is incorrect. The entire clinical trial, including design, execution, and follow-up, was performed by Dr. Liu's clinical team at Zhongshan Ophthalmic Center, Sun Yatsen University in China, and it was approved by an IRB in China. In fact, that work was completed in 2013, *before* my involvement with the research. My role consisted of analyzing the study results derived by Dr. Liu's team *after* the study was completed. As such, I was not involved in the human subject study in any way, and UCSD IRB approval was neither appropriate nor required.
If you have further questions about the clinical work described in the *Nature* article, I am confident that Dr. Liu would be happy to address them.

Sincerely,
Dr. Kang Zhang
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Jill Castellano <jillcastellano@inewsource.org>

UCSD review process

Jill Castellano <jillcastellano@inewsource.org> Sun, Jul 21, 2019 at 9:59 AM
To: Kang Zhang <kang.zhang@gmail.com>

Hi Dr Zhang,

Thanks again. The reason I have called it your study is because the paper says you designed the study and wrote the manuscript (along with two others). You were also the lead author on the reply to the letters sent to Nature. And your contact information was listed on both the original article and the reply.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6061995/
Author Contributions:
"Y.L, R.M. and **K.Z. designed the study** and wrote the paper ..."

Is this description incorrect?

Thank you,
Jill

—
Jill Castellano
Investigative Data Reporter, inewsource
Sent from my iPhone

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inewsource.org

Jill Castellano <jillcastellano@inewsource.org>

UCSD review process

Kang Zhang <kang.zhang@gmail.com> Sun, Jul 21, 2019 at 8:51 PM
To: Jill Castellano <jillcastellano@inewsource.org>

Dear Ms. Castellano,

The phase “designed the study” referred to organizing and analyzing the data and drawing conclusions from results in the process of writing the paper. I came to know the project only after the human clinical study had completed. Since you mentioned author contributions described in the Nature paper, please note the first sentence reads “H.L., S.H., Z.L., S.C., .X.L., L.L., B.C., Y.W. and Y.L. conducted the clinical trial,” which describes Dr Liu’s team as responsible for the clinical trial.

I was listed as the lead author on the reply to the letters sent to Nature because there can only be one author communicating with Nature on behalf of all authors, and Dr. Liu preferred me to do it due to our relative English proficiency and our expectation that primarily English language news media would be interested in further communications on the article.

Sincerely,

Dr. Kang Zhang

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Jill Castellano <jillcastellano@inewsource.org>

UCSD review process

Jill Castellano <jillcastellano@inewsource.org> Mon, Jul 22, 2019 at 9:54 AM
To: Kang Zhang <kang.zhang@gmail.com>

Hi Dr. Zhang,

Thanks again for your reply. Unfortunately I am still somewhat confused -- the response in Nature, which lists you as the lead author, says "the author list of the Reply comprises those authors involved in clinical investigation of lens regeneration. Those authors of the original paper who were not involved in animal and cell culture experiments and did not contribute to this response are not listed here."

Doesn't that mean you were involved in the clinical investigation?

I want to add that Nature's editorial policies state that all co-authors "have agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, **even ones in which the author was not personally involved**, are appropriately investigated, resolved, and the resolution documented in the literature."

Also, it looks like you are one of two corresponding authors along with Liu on the original study. According to Nature's editorial policies: "It is expected that the corresponding author (and on multi-group collaborations, at least one member of each collaborating group, usually the most senior member of each submitting group or team, who accepts responsibility for the contributions to the manuscript from that team) will be responsible for the following with respect to data, code and materials: (adapted from McNutt et al., Proceedings of the National Academy of Sciences, Feb 2018, 201715374; DOI: 10.1073/pnas.1715374115; licensed under CC BY 4.0):

- ensuring that data, materials, and code comply with transparency and reproducibility standards of the field and journal;
- ensuring that original data/materials/code upon which the submission is based are preserved following best practices in the field so that they are retrievable for reanalysis;
- confirming that data/materials/code presentation accurately reflects the original;
- foreseeing and minimizing obstacles to the sharing of data/materials/code described in the work
- ensuring that all authors (or group leaders in multi-lab collaborations) have certified the author list and author contributions"

I'm pointing this out because these policies seem to say that you bear a substantial responsibility for the work — including the work performed on the infants, even if you were not involved in the clinical investigation — because you are listed as a co-author and a corresponding author.

Please let me know if I'm misunderstanding something. Thank you for your replies.

Best,
Jill Castellano

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